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MEDICAL ADVISORY COMMITTEE

Report on Amœbic Dysentery and other protozoal infections of the intestine.

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MEDICAL ADVISORY COMMITTEE.

AMŒBIC DYSENTERY AND OTHER PROTOZOAL INFECTIONS OF THE INTESTINE.

Copy of reports made to Director, Medical Services, Egypt, October 1916.

We have the honour to report that Lieutenant-Colonel C. M. Wenyon has forwarded to the Committee a report on the work which he, in conjunction with Captain F. W. O'Connor, R.A.M.C., has carried out at Alexandria since February last, namely, the investigation of carriers of *Entamœba histolytica* and other intestinal protozoa, the effect of different methods of administration of emetin in amœbic dysentery cases and in carriers of *Entamœba histolytica*, and kindred subjects.

The report covers a large field of work, and is necessarily detailed and of considerable length. It has seemed most convenient that Lieutenant-Colonel Wenyon should send it direct to the War Office, so that the steps necessary for its printing and publication may be taken in London.* Lieutenant-Colonel Wenyon has, however, prepared the abstract submitted below, in regard to the principal matters which the report contains. In forwarding this, the Committee desires to lay particular stress on one or two points which emerge from this enquiry and are fully dealt with in the report itself.

1. Healthy carriers of *Entamœba histolytica* have been found to be relatively so numerous among British troops in Egypt and among samples of the native population of Egyptian cities as to render it a practical impossibility to adopt, for men in Egypt, any general preventive measures against amœbic dysentery which depends upon the detection of the amœbic carrier and his isolation until cured of his carrier condition.

The advantage, in prevention of disease, which would result from the routine examination of all convalescents to detect entamœbic carriers has also been considered. If in the case of all convalescents, or even only of all "dysentery" convalescents, special measures were taken for the above purpose, and all the entamœbic carriers segregated, the procedure could not be expected to influence perceptibly the total amount of amœbic infection from all sources to which troops in Egypt are at present exposed.

2. For the prevention of the disease in Egypt primary reliance must still be placed on general methods of sanitation which prevent human excrement of whatever origin from being exposed to flies or otherwise contaminating food, gaining access to water, or being swallowed in dust. All such measures should be applied with the greatest practicable thoroughness amongst native populations in the vicinity of camps. From this point of view, the importance of military action to strengthen the civil sanitary administration of Alexandria and Cairo, and to enforce elementary sanitary requirements in native villages and compounds which are adjacent to the desert camps, cannot be too strongly emphasised.

3. Considerations (1) and (2) apply to a large extent also to men who arrive or have arrived in England, France, and elsewhere after stay in Egypt. If all convalescents on return to England from Egypt were specially examined to detect entamœbia carriers, the numbers of carriers so dealt with would still be small compared with the carriers among returned healthy men, who would pass undetected.

4. The healthy carrier of *Entamœba histolytica* even when (as is often the case) he is not known ever to have had dysentery, may be more liable than other healthy men to be attacked by this disease, whilst his carrier condition persists. It is possible also that any such liability would be increased materially should he be sent to conditions of active service where he meets with special privations in diet, or is subject to other causes of intestinal irritation. Hence, though it is impracticable, and in our view unnecessary, from a military standpoint to search out and cure all such carriers, it is still desirable in the men's personal interest to endeavour to cure the carrier condition in

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* See R. A. M. C. Journal, January 1917, *et seq.*

individual cases whenever there is opportunity; for example, when men are in hospital or detained for other causes.

5. The strict and prolonged tests applied by Lieutenant-Colonel Wenyon and Captain O'Connor show that in healthy carriers the administration of emetin by the "Group 3" method described below was uniformly effective; the other methods described, though frequently effective, were less certain.

6. The patient recovering from an attack of undoubted amœbic dysentery, is especially liable to relapses of the disease. The methods of emetin treatment described in the report, thorough as they are, very frequently do not suffice to prevent relapse occurring within a few weeks of the treatment having ceased. It is advisable therefore in these cases to maintain an observation period, say one month after completion of the emetin treatment, and to return the case as a convalescent or fit for duty only if no relapse has occurred during that interval.

7. The question arises whether dysentery convalescents in general coming under observation on return to England should, in all cases, be detained in order to sort out, for subsequent special treatment, all those whose stools show *Entamœba histolytica* cysts or other protozoal infections. The writers of the report, assuming that it is of the greatest importance at the present time to avoid keeping fit men from duty, point out that the above procedure is often not immediately demanded for the men's military efficiency, nor is it indispensable as a measure of prevention. In their view the better practical guide is the clinical condition of a convalescent; those men only being detained for special observation whose stools are abnormal or who are obviously still in bad health.

We have the honour to be,

Sir,

Your obedient Servants,

ANDREW BALFOUR, Lt.-Col., R.A.M.C.

G. S. BUCHANAN, Lt.-Col., R.A.M.C.

J. C. G. LEDINGHAM, Lt.-Col., R.A.M.C.

C. M. WENYON, Lt.-Col., R.A.M.C.

MESOPOTAMIA:
7th October 1917.

A SUMMARY OF A REPORT BY LIEUTENANT-COLONEL C. M. WENYON AND CAPTAIN F. W. O'CONNOR

Entitled

"*An enquiry into some problems affecting the spread and incidence of intestinal protozoal infections of British troops and natives in Egypt; with special reference to the carrier question, diagnosis and treatment of amœbic dysentery and an account of three new human intestinal protozoa.*"

Examinations of healthy and convalescent troops in camp and such men in hospital were undertaken in order to discover how widespread were the *Entamœba histolytica* infections. Nearly two thousand (1,979) healthy troops were examined and these gave a percentage of 5·3 for the *Entamœba histolytica* carriers. Convalescent patients in the Mustapha Depôt gave a slightly higher figure. A uniform system was adopted by which all the results are based on a single examination or on the first only of several observations. Experience shows that this is reasonably constant for comparative purposes though it does not represent the actual carriers which would be found if repeated examinations had been made in all cases. In one series of 97 men it was found that the figures given by a single examination had to be multiplied by three to approximate total carriers. It was evident that a high percentage of *Entamœba histolytica* carriers existed amongst the troops in Egypt. It was thought that the cause of the infection must be the native and this view was confirmed by the examination of over five hundred (524) natives in the Hadra Prison at Alexandria. Of these men 13·7 per cent. were carriers of *Entamœba histolytica*. We have shown, not only experimentally, but by the examination of wild flies caught in Alexandria, that these insects are probably responsible in large degree for the spread of infection from the native to the newly arrived British soldier. As there are so many carriers amongst the healthy and convalescent soldiers it is evident that it is imposible to attempt the identification of all carriers amongst a large body of men. It is likewise clear that large numbers of carriers must have been included in course of the frequent transferences of healthy troops from Egypt to England, France and elsewhere Similarly with the invaliding of convalescents to England an almost equal percentage of carriers is being introduced amongst them. When they reach England the majority of the convalescents have completely recovered from their dysentery or other illness.

It is evident that if a systematic examination of these men is made, carriers of *Entamœba histolytica* will be discovered amongst them. It seems to us that as no examination of healthy troops can possibly be undertaken with a view to the isolation of the large number of carriers amongst them, so examination of recovered convalescents for the same purpose becomes unnecessary. The removal of the convalescents will do practically nothing to reduce the percentage of carriers amongst the healthy troops. We would advocate the examination only of such convalescents as have not completely recovered and are found to be still passing abnormal stools after proper inspection or who cannot take a full diet. A similar rule can be followed with regard to men infected with flagellates (lamblia, tetramitus, trichomonas). If the men have recovered it is unnecessary to subject the stool to microscopic examination. This need only be done in the case of men who are still passing abnormal stools or are ill in any other way and thus unfit to return to duty. Of other protozoal infections in Egypt that of *Entamœba coli* is by far the commonest. The small *Entamœba nana* is often met with while, of the flagellates, lamblia, tetramitus and trichomonas, the first named is most frequently seen.

The following is a composite table showing the percentage of protozoal infections met with amongst various groups of men examined in Alexandria and London :—

—	Healthy troops.	Convalescents, Alexandria.	Gallipoli, convalescents in London October-December 1915.	Hospital cases.	Gabarri British Prison.	Hadra Prison, Natives.	Alexandria restaurant Native cooks military.	British West Indian cooks, Gabarri.
Total examined . . .	1,979	128	556	961	168	524	87	48
E. histolytica . . .	5·8	6·4	10·8	3·2	1·8	13·7	11·5	4·1
E. coli	20·0	31·7	39·0	10·4	12·0	48·6	20·7	18·7
Lamblia	4·8	5·4	16·0	6·0	6·0	0·57	7·0	4·1
Trichomonas	1·1	0·67	1·6	3·0	2·4	...	1·1	...
Tetramitus	1·1	0·9	0·7	2·8	3·2	0·19	1·1	...
Coccidium (Isospora) . .	...	...	2·7	...	...	...	...	...
Cocoidium (Eimeria) . .	...	...	0·2	...	...	...	...	...
Entamoebae, undiagnosed .	1·3	1·8	...	2·0	17·2	0·57	1·1	...
Iodine cysts	3·0	2·0	5·2	0·3	...	14·8	7·0	4·1
E. nana	...	...	1·0	3·0	12·0	...	...	...

Difficulty attending the diagnosis of *Entamœba histolytica* in the stool undoubtedly exists and the following rules for guidance are put forward :—

1. If amœbæ containing red blood corpuscles are present in the stool, whether evidently dysenteric or not, they are *Entamœba histolytica* and mean that some active dysenteric process is going on.

2. If the actual amœbic dysenteric process is so acute as to demand immediate emetin treatment, then amœbæ with included red blood corpuscles will almost certainly be present in the stool.

3. If amœbæ, none of which contain red blood corpuscles, are present in a dysenteric stool then the case is either (*a*) bacillary dysentery (or other form of dysentery) with an infection of *Entamœba coli* or (*b*) bacillary dysentery (or other form of dysentery) occurring in a carrier case of *Entamœba histolytica* in which there is no active amœbic dysenteric process in progress.

4. In either case mentioned under 3 no anti-amœbic treatment is urgent, so that the case can be watched for a few days during which encysted forms of *Entamœba coli* or *Entamœba histolytica* will almost certainly appear as the acute symptoms subside, and the diagnosis will be established.

5. Amœbæ, none of which contain red blood corpuscles and which occur in non-dysenteric stools, may be either *Entamœba coli* or *Entamœba histolytica.* In such cases, cysts are nearly always associated with the amœbæ, but, if not, treatment for the amœbic infection being never urgent or not required at all, the diagnosis can be made by daily examination extending over a few days till cysts appear, as they almost invariably do It sometimes, though rarely, happens that amœbæ cannot be found in the stool, even after several examinations, when active amœbic ulceration of the large intestine is present.

The cysts of *Entamœba histolytica* are as a rule not difficult to identify. We have found, however, that there is a greater range in size than was formerly supposed. In fact, distinct strains of *Entamœba histolytica* exist. In some, the cysts are quite small, being only 7 to 9 microns in diameter. In others, the cysts are large having a diameter of 14 to 19 microns, but most frequently the cyst measures 10 to 14 microns. The mature cyst always has a maximum of four nuclei. There cannot be any doubt that the presence of these cysts in the stool is an indication of infection with *Entamœba histolytica* even when there has been no history of dysentery. The reasons for this condition may be tabulated thus :—

1. Cases which are passing cysts of *Entamœba histolytica* may relapse into acute dysentery when amœbæ with included red blood corpuscles appear in the stool.

2. Cases of amœbic dysentery showing amœbæ with included red blood corpuscles may recover naturally, and in the process the large active amœbæ become replaced by smaller amœbæ and cysts of *Entamœba histolytica.*

3. Cases of acute amœbic dysentery of the above type may be cured with emetin but they frequently relapse as evidenced by the appearance of cysts of *Entamœba histolytica* in the stool to be followed by an attack of acute dysentery.

4. Cysts from perfectly healthy carrier cases who have no previous history of dysentery can give rise to fatal amœbic dysentery in kittens.

Carriers of *Entamœba histolytica* may remain infected for as long as five years during which they may have repeated attacks of dysentery. We do not know if every *Entamœba histolytica* carrier is doomed to dysenteric attacks but we know that a certain percentage are. It is perfectly clear that a large percentage of men who are stationed even for a short time in Egypt become infected with *Entamœba histolytica.* A certain, still unknown, though by no means negligible, percentage of these pass on to a condition of amœbic dysentery and have to be invalided from the service. It is evident, therefore, that in the transference of new troops from England to non-infected centres it is inadvisable to station them in the first place in endemic centres of amœbic dysentery like Egypt unless important military requirements leave no other alternative. It seems possible that most individuals who become infected with *Entamœba histolytica* do so without having any symptoms and when they first have an attack of dysentery they have already been carriers of the amœbæ for a varying period. A few, however, appear to suffer from actual dysentery very soon after infection. Unfortunately no definite statement can be made as to what proportion of carriers ultimately become actual dysenterics. The stool of the bacillary dysenteric, if seen in the blood and mucus stage, can generally be recognised and distinguished from that of amœbic dysentery by the great abundance of pus and other cells. The large cells, so often mistaken for amœbæ, may actually ingest red blood corpuscles. They are probably derived from the endothelium of blood vessels and may be called macrophages.

The difficulty attending the recognition of unencysted *Entamœba coli* are as great as those mentioned above for *Entamœba histolytica*. *Entamœba coli* may actually ingest cysts of *Entamœba histolytica*. We could obtain no evidence, after observation on undoubted *Entamœba coli* infections and on cases of bacillary dysentery associated with these amœbæ, that *Entamœba coli* could ingest red blood corpuscles or that it was ever pathogenic. The cysts of *Entamœba coli* vary greatly in size. The smallest we have seen had diameters of 13 microns. The largest measured 38 × 34 microns.

Of all the flagellates of the human intestine, lamblia has the greatest claim to pathogenicity. It may remain in the intestine for years and give rise to attacks of diarrhœa when quantities of mucus are passed. The flagellate reproduces by longitudinal division. These dividing forms have been seen for the first time. Tetramitus infections may be recognised by the finding of cysts in the stool. Infections with this flagellate and with trichomonas are very persistent but their pathogenicity is somewhat doubtful. Two new human intestinal flagellates, *Waskia intestinalis* and *Tricercomonas intestinalis* and a new entamœba, *Entamœba nana* are described for the first time. As far as we have been able to determine, they have no pathological significance.

Treatment of Entamœba histolytica and other protozoal infections.

In the treatment of *Entamœba histolytica* infections, emetin hydrochloride has been almost exclusively used. A few cases were treated with methyl emetin sulphate. The cases were arranged in three groups according to the method of emetin administration. During the stay in hospital the stools were examined macro and microscopically every day. After treatment was finished, the patient went to a convalescent depôt (Mustapha) where he remained at least one month. During this period the stool was examined microscopically every other day. In this manner it was possible to detect a relapse as soon as it occurred. This happened in under twenty days in all cases which relapsed, with the exception of three which relapsed in under thirty days.

Group 1.—Injection of one grain of emetin each day for 12 days—

A. *Carrier cases.*—52 were treated, of these 37 were cured, 10 relapsed and in 5 there was no reaction to treatment, six of the uncured cases were eventually cured by treatment in group 3 (*vide infra*).

B. *Acute cases.*—6 were treated and all relapsed. One of the acute cases was eventually cured by treatment in group 3 (*vide infra*).

In this group the carrier cases were not confined to bed and had chicken diet. The acute cases were kept in bed on dysentery diet. A sodium sulphate mixture was given regularly three or four times a day.

Group 2.—Administration of emetin by the mouth one grain daily for twelve days.

A. *Carrier cases.*—9 were treated, of these 6 were cured, 2 relapsed and 1 did not react to treatment.

B. *Acute cases.*—3 were treated, of these 2 relapsed and 1 did not react to treatment.

The cases were handled as in group 1 except that the saline was not administered so regularly.

In addition to the above, one acute case relapsed after treatment with half a grain of emetin by the mouth for twelve days. A carrier case did not react to one and a half grains of emetin by the mouth for twelve days while another was cured by orally-administered emetin, one grain a day for 2 days followed by ½ grain a day for 7 days. Yet another was cured by 1½ grains a day for 4 days followed by1 grain for eight days (coral administration).

Group 3—Emetin 1½ grains a day for twelve days (one grain injection each morning and ½ grain by the mouth at night in keratin (coated tabletion).

A. *Carrier cases*—30 were treated and all were cured.

B. *Acute cases*—7 were treated and 2 were cured while 5 relapsed. In this group all cases were kept in bed on milk or dysentery diet. The saline mixture was rarely given, as orally administered emetin tends to keep the bowels loose.

Comparison of results in groups 1, 2 & 3.

——	Group 1.	Group 2.	Group 3.
Carrier cases cured	37	6	30
Carrier cases relapsed	10	2	...
Carrier cases no reaction	5	1	...
Acute cases cured	...	...	2
Acute cases relapsed	6	2	5
Acute cases no reaction	...	1	...

In 37 cured cases in group 1, the infection disappeared on an average in 4 days.

In 30 cured cases in group 3, the infection disappeared on an average in 2 days.

From these figures it is evident that the best result are obtained by treatment as in Group 3. The carrier cases were all cured. The acute cases with actual amœbic dysentery and generally with histories of repeated attacks are difficult to treat successfully. It is suggested that the acute cases with tendency to relapse might be given, after the initial course, a prolonged treatment by small doses of emetin ⅙ or even ¼ of a grain a day by the mouth.

In the handling of *E. histolytica* infections, it is not the presence of cysts which makes treatment difficult but rather the degree and character of the ulceration of the large intestine. One of the most resistant cases never showed cysts at any time during a three months' observation while there was undoubtedly extensive ulceration of the large intestine. The latter is most marked and has been of longest duration in the cases which give histories of repeated attacks of dysentery. It is least extensive in the healthy carriers who give no history of dysentery. There does not appear to be any evidence that inadequate emetin treatment increases the number of carriers nor that emetin tends to make encysted forms appear in the stool. In the treatment of carrier cases it is not the cysts we attack but the amœbæ which are producing the cysts. As far as we have been able to judge emetin-resistant strains of *Entamœba histolytica* do not exist.

The majority of cases of *Entamœba histolytica* treated by us showed also other protozoal infections [*E. coli*, lamblia, trichomonas, tetramitus]. The action of emetin on *Entamœba histolytica* was not influenced in any way by the presence of other protozoa.

In only two cases did the emetin appear to act deleteriously on the heart. Both these cases had been given two 12 day courses of emetin with only a few days' interval. Upon getting up after the second course, both cases showed symptoms of heart trouble—shortness of breath, rapid pulse and irregular heart action on slight exertion. The condition passed off in two or three weeks. Methylemetin sulphate was tried in three acute cases and one carrier in a twelve day course. The dose employed was one grain injection each morning and one grain in keratin coated tablet by the mouth each night. Of the acute cases two relapsed and one did not even react to treatment. The single carrier case was cured. The methyl-emetin by the mouth does not cause vomiting like the emetin hydrochloride. Very little can be done in the way of ridding an individual of other protozoal infections. Emetin, when given as in Group 3 [one grain injection each morning and $\frac{1}{2}$ grain by the mouth at night), usually abolishes temporarily all concurrent protozoal infections. They all return later however. Flagellate infections can generally be got rid of by means of bismuth salicylate, grains 20, t. d. s. When the treatment is stopped after a twelve or fifteen-day course the infections usually re-appear. Prolonged treatment by this drug may give better results.

One coccidium [Isospora] infection was abolished by emetin treatment as in Group 3. There was no relapse.

S. G. P. I., Delhi—No. 1501 D. M. S. I.—12-3-17.—50.